

CLAIMS

What is claimed is:

1. A compound of formula (I):



5

(I)

or a pharmaceutically acceptable salt thereof,

wherein

the α -nitrogen of AA¹, AA², AA³, AA^{3b}, AA⁴, AA⁵, AA⁶, AA⁷, AA^{7b}, and AA⁸ each is, independently, optionally substituted with (C₁₋₄)alkyl, (C₃₋₄)alkenyl, (C₃₋₄)alkynyl, or (C₁₋₆)alkyl-C(O)-;

AA¹ is absent or the D- or L-isomer of an amino acid selected from the group consisting of R¹¹, Aac, Aic, Arg, Asn, Asp, Dip, Gln, Glu, Hca, Hyp, Lys, Mac, Macab, Orn, Pro, Ser, Ser(Bzl), Thr, Thr(Bzl), Pip, hArg, Bip, Bpa, Tic, Cmp, Inc, Inp, Nip, Ppc, Htic, Thi, Tra, Cmpi, Tpr, Iia, Alla, Aba, Gba, Car, Ipa, Iaa, Inip, Apa, Mim, Thnc, Sala, Aala, Thza, Thia, Bal, Fala, Pala, Dap, Agly, Pgly, Ina, Dipa, Mnf, Inic, C4c, 5-Iqs, Htqa, 4-Mqc, Thn, α -Chpa, Cit, Nua, Pyp and an optionally substituted aromatic α -amino acid;

wherein said optionally substituted aromatic α -amino acid is optionally substituted with one or more substituents each independently selected from the group consisting of halogen, NO₂, OH, CN, (C₁₋₆)alkyl, (C₂₋₆)alkenyl, (C₂₋₆)alkynyl, (C₁₋₆)alkoxy, Bzl, O-Bzl, and NR⁹R¹⁰;

AA² is absent or the D- or L-isomer of an amino acid selected from the group consisting of R¹¹, Aic, Arg, Hca, His, Hyp, Pal, F₅-Phe, Phe, Pro, Trp, and X⁰-Phe Pip, hArg, Bip, Bpa, Tic, Cmp, , Inc, Inp, Nip, Ppc, Htic, Thi, Tra, Cmpi, Tpr, Iia, Alla, Aba, Gba, Car, Ipa, Iaa, Inip, Apa, Mim, Thnc, Sala, Aala, Thza, Thia, Bal, Fala, Pala, Dap, Agly, Pgly, Ina, Dipa, Mnf, Inic, I-Iqc, 3-Iqc, C4c, 5-Iqs, Htqa, 4-Mqc, Thn, α -Chpa, Cit, Nua, and Pyp;

AA³ is the D- or L-isomer of an amino acid selected from the group consisting of Cys, hCys, Pen, Tpa, Tmpa, Mac, Macab, and an optionally substituted aromatic α -amino acid;

wherein said optionally substituted aromatic α -amino acid is optionally substituted with one or more substituents selected from the group consisting of halogen, NO₂, OH, CN, (C₁₋₄)alkyl, (C₂₋₄)alkenyl, (C₂₋₄)alkynyl, (C₁₋₄)alkoxy, Bzl, O-Bzl, NR⁹R¹⁰, Pip, hArg, Bip, Bpa, Tic, Cmp, , Inc, Inp, Nip, Ppc, Htic, Thi, Tra, Cmpi, Tpr, , Iia, Alla, Aba, Gba, Car, Ipa, Iaa, Inip, Apa, Mim, Thnc, Sala, Aala, Thza, Thia, Bal, Fala, Pala, Dap, Agly, Pgly, Ina, Dipa, Mnf, Inic, 10 I-lqc, 3-lqc, C4c, 5-lqs, Htqa, 4-Mqc, Thn, α -Chpa, Cit, Nua, and Pyp; AA^{3b} is absent or the D- or L-isomer of an amino acid selected from the group consisting of Pal, 4-Pal, His, Arg, Nal, Trp, Bpa, F₅-Phe, Phe, X⁰-Phe, R¹¹, hArg, Bip, Tic, , Htic, Dip, Sala, Aala, Thza, Thia, Bal, Fala, and Pala;

AA⁴ is a D- or L-isomer of an optionally substituted amino acid or of an 15 optionally substituted aromatic α -amino acid;

wherein said optionally substituted amino acid is selected from the group consisting of Trp, Lys, Orn, hLys, *cis*-4-Acha, *trans*-4-Acha, *trans*-4-Amcha, 4-Pip-Gly, N-Met-Trp, β -Met-Trp, His, hHis, hArg, Bip, Tic, Htic, Dip, Sala, Aala, Thza, Thia, Bal, Fala, Pala, and 4-Pip-Ala;

wherein the side chain amino group of said optionally substituted amino 20 acid is optionally substituted with R³ and R⁴; and

wherein said optionally substituted aromatic α -amino acid is optionally substituted with one or more substituents each independently selected from the group consisting of halogen, NO₂, OH, CN, (C₁₋₄)alkyl, (C₂₋₄)alkenyl, (C₂₋₄)alkynyl, Bzl, O-Bzl, and NR⁹R¹⁰;

AA⁵ is absent, R¹¹, Aic, A3c, A4c, A5c, A6c, Abu, Aib, β -Ala, Bpa, Cha, Deg, Gaba, Ile, Leu, Nal, Nle, Pro, Sar, Ser, Ser(Bzl), Thr, Thr(Bzl), Trp, Val, Pal, F₅-Phe, Phe, X⁰-Phe, or an optionally substituted D- or L- isomer of an amino acid selected from the group consisting of 4-Pip-Gly, 4-Pip-Ala, *cis*-4-Acha,

trans-4-Acha, *trans*-4-Amcha, hLys, Lys, Orn, hArg, Bip, Tic, , Htic, Dip, Sala, Aala, Thza, Thia, Bal, Fala, and Pala; wherein the side-chain amino group of said optionally substituted amino acid is optionally mono- or di-substituted with R³ and R⁴;

5 AA⁶ is absent or the D- or L-isomer of an amino acid selected from the group consisting of R¹¹, an optionally substituted aromatic α -amino acid, Cys, hCys, Pen, Tpa, Tmpa, Thr, Thr(Bzl), Ser, Ser(Bzl), hArg, Bip, Tic, , Htic, Dip, Sala, Aala, Thza, Thia, Bal, Fala, and Pala;

AA⁷ is absent or the D- or L-isomer of an amino acid selected from the group

10 consisting of R¹¹, an optionally substituted aromatic α -amino acid, A3c, A4c, A5c, A6c, Abu, Aib, Aic, β -Ala, Arg, Cha, Deg, Gaba, Ile, Leu, Nle, Pip, Pro, Sar, Ser, Ser(Bzl), Thr, Thr(Bzl), Val, Tic, Htic, Sala, Aala, Thza, Thia, Bal, Fala, Pala, hArg, Bip, Bpa, Dip, Pal, Sala, and X⁰-Phe;

AA^{7b} is absent or a D- or L-isomer of an amino acid selected from the group

15 consisting of R¹¹, Bpa, Phe, F₅-Phe, X⁰-Phe, Nal, Pro, Ser, Ser(Bzl), Thr, Thr(Bzl), Trp, hArg, Bip, Tic, Htic, Dip, Sala, Aala, Thza, Thia, Bal, Fala, and Pala;

AA⁸ is absent or the D- or L- isomer of an amino acid selected from the group consisting of R¹¹, Maa, Maaab, Thr, Thr(Bzl), Ser, Ser(Bzl), Tyr, Phe(4-O-Bzl), F₅-Phe, and X⁵-Phe, and an optionally substituted aromatic α -amino acid;

20 R¹ and R² each is, independently, H, E-, E(O)₂S-, E(O)C-, EOOC-, R¹³, or absent;

R³ and R⁴ each is, independently, (C₁₋₁₂)alkyl, (C₂₋₁₂)alkenyl, (C₂₋₁₂)alkynyl, phenyl, naphthyl, phenyl-(C₁₋₆)alkyl, phenyl-(C₂₋₆)alkenyl, phenyl-(C₂₋₆)alkynyl, naphthyl-(C₁₋₆)alkyl, naphthyl-(C₂₋₆)alkenyl, naphthyl-(C₂₋₆)alkynyl, (cyclo(C₃₋₇)alkyl)-(C₁₋₆)alkyl, (cyclo(C₃₋₇)alkyl)-(C₂₋₆)alkenyl, (cyclo(C₃₋₇)alkyl)-(C₂₋₆)alkynyl, heterocyclyl-(C₁₋₄)alkyl, heterocyclyl-(C₂₋₄)alkenyl, heterocyclyl-(C₂₋₆)alkynyl,

- 56 -

X^4 alkynyl, 1-adamantyl, 2-adamantyl, 9-fluorenylmethyl, dicyclopropylmethyl, dimethylcyclopropylmethyl, or benzhydryl;

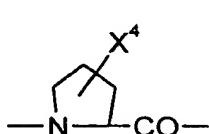
R^5 is $-OR^6$, $-NR^7R^8$, or absent,

wherein each R^6 , R^7 and R^8 is, independently, H, (C_{1-12}) alkyl, (C_{2-12}) alkenyl,

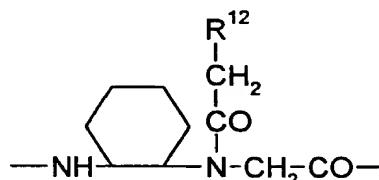
5 (C_{2-12}) alkynyl, phenyl, naphthyl, phenyl- (C_{1-6}) alkyl, phenyl- (C_{2-6}) alkenyl, phenyl- (C_{2-6}) alkynyl, naphthyl- (C_{1-6}) alkyl, naphthyl- (C_{2-6}) alkenyl, naphthyl- (C_{2-6}) alkynyl, 1-adamantyl, 2-adamantyl, 9-fluorenylmethyl, dicyclopropylmethyl, dimethylcyclopropylmethyl, or benzhydryl;

10 R^9 and R^{10} each is, independently, H, (C_{1-6}) alkyl, (C_{3-4}) alkenyl, (C_{3-4}) alkynyl, 1-adamantyl, or 2-adamantyl;

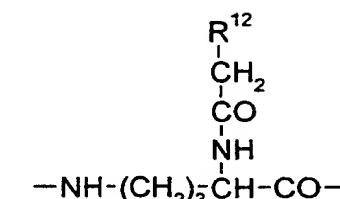
R^{11} is, independently for each occurrence, a D- or L-amino acid of the formula:



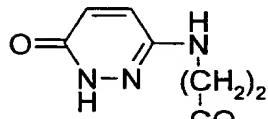
(1)



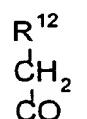
(2)



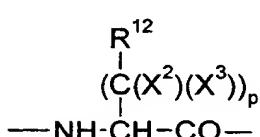
(3)



(4)



(5)



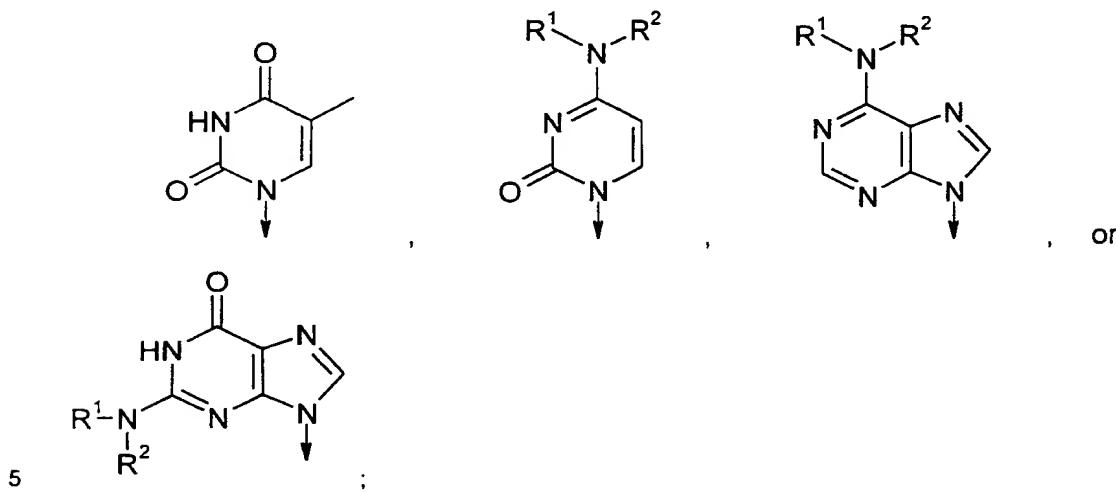
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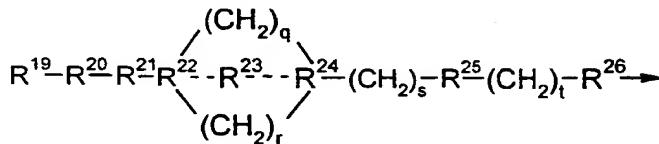
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- 57 -

wherein m and n each is, independently, 1, 2, or 3, and p is 0, 1, or 2;
 R¹² is, independently for each occurrence, an optionally substituted moiety of
 the formula:



R¹³ is a moiety of the formula



wherein q, r, s, and t each is, independently, 0, 1, 2, 3, 4 or 5;
 R¹⁹ is absent, H, NH₂, OH, (C₁₋₆)hydroxyalkyl, N(R²⁷R²⁸), SO₃H, or an
 10 optionally substituted moiety selected from the group consisting of
 heterocyclyl, phenyl and naphthyl,

wherein the optionally substituted moiety defined for R¹⁹ is optionally
 substituted with one or more substituents selected, independently for each
 occurrence, from the group consisting of halogen, NO₂, OH, (C₁₋₆)alkyl,
 15 (C₂₋₆)alkenyl, (C₂₋₆)alkynyl, (C₁₋₆)alkoxy, NH₂, mono- or di-(C₁₋₆)alkylamino,
 Bzl, and O-Bzl;

R²⁰ is O or absent;

R²¹ is (C₁₋₆)alkyl or absent;

- 58 -

R²² is N, O, C, or CH;

R²³ is (C₁₋₆)alkyl or absent;

R²⁴ is N, CH, or C;

R²⁵ is NH, O, or absent;

5 R²⁶ is SO₂, CO, or CH;

R²⁷ and R²⁸ each is, independently, H or (C₁₋₆)alkyl;

E is, independently for each occurrence, an optionally substituted moiety selected from the group consisting of (C₁₋₁₂)alkyl, (C₂₋₁₂)alkenyl, (C₂₋₁₂)alkynyl, phenyl, naphthyl, phenyl-(C₁₋₆)alkyl, phenyl-(C₂₋₆)alkenyl, phenyl-(C₂₋₆)alkynyl,

10 naphthyl-(C₁₋₆)alkyl, naphthyl-(C₂₋₆)alkenyl, naphthyl-(C₂₋₆)alkynyl, (cyclo(C₃₋₇)alkyl)-(C₁₋₆)alkyl, (cyclo(C₃₋₇)alkyl)-(C₂₋₆)alkenyl, (cyclo(C₃₋₇)alkyl)-(C₂₋₆)alkynyl, heterocyclyl-(C₁₋₄)alkyl, heterocyclyl-(C₂₋₄)alkenyl, heterocyclyl-(C₂₋₄)alkynyl, 1-adamantyl, 2-adamantyl, dicyclopropylmethyl, dimethylcyclopropylmethyl, 9-fluorenylmethyl, and benzhydryl;

15 wherein the optionally substituted moiety defined for E is optionally substituted with one or more substituents each independently selected from the group consisting of halogen, OH, Bzl, O-Bzl, NO₂, CN, COOH, and SH;

X⁰ is halogen, NO₂, OH, (C₁₋₆)alkyl, (C₁₋₆)alkoxy, mono- or di-(C₁₋₆)alkylamino, Bzl, O-Bzl, NR⁹R¹⁰, or CN;

20 X¹ is H, (C₁₋₆)alkyl, (C₂₋₆)alkenyl, (C₂₋₆)alkynyl, indolyl, imidazolyl, 1-naphthyl, 3-pyridyl, optionally ring-substituted benzyl, or a moiety which corresponds to the side-chain group of Arg, Leu, Gln, Lys, Tyr, His, Thr, Trp, Phe, Val, Ala, Lys, or His;

25 wherein said optionally ring-substituted benzyl is optionally substituted with one or more substituents selected from the group consisting of halogen, OH, (C₁₋₆)alkoxy, mono- or di-(C₁₋₆)alkylamino, (C₁₋₄) alkyl, (C₂₋₄) alkenyl, (C₂₋₄) alkynyl, and NR⁹R¹⁰;

- 59 -

X² and X³ each is, independently, H, halogen, OH, =O, =S, (C₁₋₁₂)alkyl, (C₂₋₁₂)alkenyl, (C₂₋₁₂)alkynyl, phenyl, naphthyl, phenyl-(C₁₋₆)alkyl, phenyl-(C₂₋₆)alkenyl, phenyl-(C₂₋₆)alkynyl, naphthyl-(C₁₋₆)alkyl, naphthyl-(C₂₋₆)alkenyl, naphthyl-(C₂₋₆)alkynyl, (cyclo(C₃₋₇)alkyl)-(C₁₋₆)alkyl, (cyclo(C₃₋₇)alkyl)-(C₂₋₆)alkenyl, (cyclo(C₃₋₇)alkyl)-(C₂₋₆)alkynyl, heterocyclyl-(C₁₋₄)alkyl, heterocyclyl-(C₂₋₄)alkenyl, heterocyclyl-(C₂₋₄)alkynyl, 1-adamantyl, 2-adamantyl, dicyclopropylmethyl, or dimethylcyclopropyl methyl;

X⁴ is H, OH, or NH₂; and

X⁵ is halogen, NO₂, CH₃, OH, Bzl or O-Bzl;

10 provided that:

at least six amino acid residues are present;

when AA³ is a D- or L-isomer of an amino acid selected from the group consisting of Cys, hCys, Pen, Tpa, or Tmpa, and AA⁶ is a D- or L-isomer of an amino acid selected from the group consisting of Cys, hCys, Pen, 15 Tpa, or Tmpa, then AA³ and AA⁶ are connected by a disulfide bond;

when AA¹ or AA³ is a D- or L-isomer of an amino acid selected from the group consisting of Mac or Macab, then AA⁸ is a D- or L-isomer of an amino acid selected from the group consisting of Maa and Maaab, and when AA⁸ is a D- or L-isomer of an amino acid selected from the group 20 consisting of Maa and Maaab, then AA¹ or AA³ is a D- or L-isomer of Mac or of Macab, and AA¹ or AA³ is connected by a disulfide bond with AA⁸;

AA² can be D- or L-Hca only when AA¹ is absent; when one of R¹ or R² is E(O)₂S-, E(O)C-, EOOC-, or R¹³, the other is H; when R⁵ is absent, then one of R¹ or R² is also absent, and the N-terminal 25 amino acid and C-terminal amino acid together form an amide bond; when one of X² or X³ is C=O or C=S, the other is absent; and said compound of formula (I) is not of the formula:

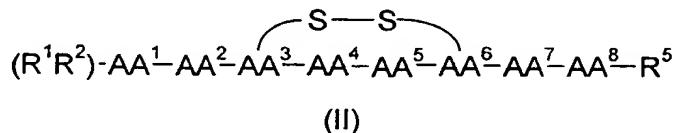
D-Phe-Tyr-cyclo(D-Cys-D-Trp-Lys-Cys)-Abu-Thr-NH₂;

Ac-Phe-Tyr-cyclo(D-Cys-D-Trp-Lys-Cys)-Abu-Thr-NH₂;

- 60 -

L-4-NO₂-Phe-Tyr-cyclo(D-Cys-D-Trp-Lys-Cys)-Abu-Thr-NH₂;
 Ac-L-4-NO₂-Phe-Tyr-cyclo(D-Cys-D-Trp-Lys-Cys)-Abu-Thr-NH₂;
 Hca-Tyr-cyclo(D-Cys-D-Trp-Lys-Cys)-Abu-Thr-NH₂;
 D-Dip-Tyr-cyclo(Cys-D-Trp-Lys-D-Cys)-Val-Nal-NH₂;
 5 D-4-NO₂-Phe-Phe(4-O-Bzl)-cyclo(D-Cys-D-Trp-Lys-Cys)Cha-Nal-NH₂;
 or
 D-4-NO₂-Phe-cyclo(D-Cys-Phe(4-O-Bzl)-D-Trp-Lys-Cys)-Val-Tyr-NH₂.

2. A compound according to claim 1, wherein said compound is of
 10 formula (II):



or a pharmaceutically acceptable salt thereof,
 wherein
 15 AA¹ is absent or the D- or L-isomer of an amino acid selected from the group
 consisting of R¹¹, Aac, Aic, Arg, Asn, Asp, Dip, Gln, Glu, Hyp, Lys, Mac,
 Macab, Orn, Pip, Pro, Ser, Ser(Bzl), Thr, Thr(Bzl), Pip, hArg, Bip, Bpa, Tic,
 Cmp, , Inc, Inp, Nip, Ppc, Htic, Thi, Tra, Cmpi, Tpr, , Iia, Alla, Aba, Gba, Car,
 Ipa, Iaa, Inip, Apa, Mim, Thnc, Sala, Aala, Thza, Thia, Bal, Fala, Pala, Dap,
 20 Agly, Pgly, Ina, Dipa, Mnf, Inic, I-Iqc, 3-Iqc, C4c, 5-Iqs, Htqa, 4-Mqc, Thn, α -
 Chpa, Cit, Nua, Pyp and an optionally substituted aromatic α -amino acid,
 wherein said optionally substituted aromatic α -amino acid is optionally
 substituted with one or more substituents selected from the group
 consisting of halogen, NO₂, OH, CN, (C₁₋₆)alkyl, (C₂₋₆)alkenyl, (C₂₋₆)alkynyl,
 25 and NR⁹R¹⁰;
 AA² is absent or the D- or L-isomer of an amino acid selected from the group
 consisting of R¹¹, Aic, Arg, Hca, His, Hyp, Pal, F₅-Phe, Phe, Pro, Trp, X⁰-Phe,
 Pip, hArg, Bip, Bpa, Tic, Cmp, , Inc, Inp, Nip, Ppc, Htic, Thi, Tra, Cmpi, Tpr, ,

lia, Alla, Aba, Gba, Car, Ipa, Iaa, Inip, Apa, Mim, Thnc, Sala, Aala, Thza, Thia, Bal, Fala, Pala, Dap, Agly, Pgly, Ina, Dipa, Mnf, Inic, I-Iqc, 3-Iqc, C4c, 5-Iqs, Htqa, 4-Mqc, Thn, α -Chpa, Cit, Nua, and Pyp; AA³ is the D- or L-isomer of an amino acid selected from the group consisting of Cys, hCys,

5 Pen, Tpa and Tmpa;

AA⁴ is a D- or L-isomer of an amino acid selected from the group consisting of Trp, N-Met-Trp, β -Met-Trp, His, hHis, hArg, Bip, Tic, , Htic, Dip, Sala, Aala, Thza, Thia, Bal, Fala, Pala, and an optionally substituted aromatic α -amino acid,

10 wherein said optionally substituted aromatic α -amino acid is optionally substituted with one or more substituents each independently selected from the group consisting of halogen, NO₂, OH, (C₁₋₄)alkyl, (C₂₋₄)alkenyl, (C₂₋₄)alkynyl, Bzl, O-Bzl, and NR⁹R¹⁰;

AA⁵ is a D- or L-isomer of an amino acid selected from the group consisting of 4-Pip-Gly, 4-Pip-Ala, *cis*-4-Acha, *trans*-4-Acha, *trans*-4-Amcha, hLys, Lys, Orn, hArg, Bip, Tic, , Htic, Dip, Sala, Aala, Thza, Thia, Bal, Fala, and Pala, wherein the side-chain amino group of said amino acid is optionally mono- or di-substituted with R³ and R⁴;

15 AA⁶ is a D- or L-isomer of an amino acid selected from the group consisting of Cys, hCys, Pen, Tpa, and Tmpa;

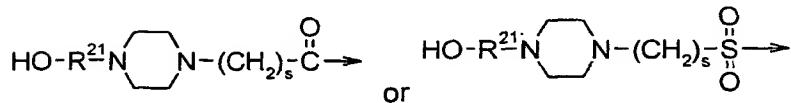
AA⁷ is absent or a D- or L-isomer of an amino acid selected from the group consisting of R¹¹, Aic, A3c, A4c, A5c, A6c, Abu, Aib, β -Ala, Arg, Bpa, Cha, Deg, Gaba, His, Ile, Leu, Nal, Nle, Pal, Phe, F₅-Phe, Pro, Sar, Ser, Ser(Bzl), Thr, Thr(Bzl), Trp, N-Me-Trp, Val, N-Me-Val, hArg, Bip, Tic, , Htic, Dip, Sala,

20 Aala, Thza, Thia, Bal, Fala, Pala, and X⁰-Phe ;

AA⁸ is absent or the D- or L-isomer of an amino acid selected from the group consisting of R¹¹, an optionally substituted aromatic α -amino acid, Maa, Maaab, Ser, Ser(Bzl), Thr, Thr(Bzl), Tyr, Phe(4-O-Bzl), F₅-Phe, and X⁵-Phe;

25 R¹³ is a moiety according to the formula

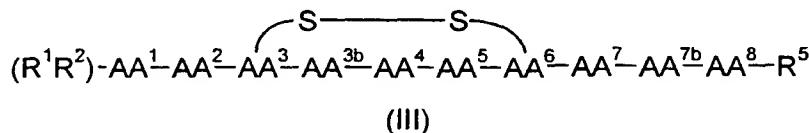
- 62 -



wherein R^{21} is (C_{1-4}) alkyl and s is 1, 2, 3, or 4; and
 X^0 is halogen, NO_2 , CH_3 , OH , Bzl , $O-Bzl$ or CN ;
provided that at least one of AA^7 or AA^8 is present.

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3. A compound according to claim 1, wherein said compound is of formula (III):



10 or a pharmaceutically acceptable salt thereof,
wherein
 AA^1 is absent or the D- or L-isomer of an amino acid selected from the group consisting of R^{11} , Aac , Aic , Arg , Asn , Asp , Gln , Glu , Hca , His , Hyp , Lys , Mac , $Macab$, Orn , Pro , Ser , $Ser(Bzl)$, Thr , $Thr(Bzl)$, Pip , $hArg$, Bip , Bpa , Tic , Cmp ,
15 $, Inc$, Inp , Nip , Ppc , $Htic$, Thi , Tra , Cmp , Tpr , Iia , $Alla$, Aba , Gba , Car , Ipa ,
 Iaa , $Inip$, Apa , Mim , $Thnc$, $Sala$, $Aala$, $Thza$, $Thia$, Bal , $Fala$, $Pala$, Dap , $Agly$,
 $Pgly$, Ina , $Dipa$, Mnf , $Inic$, $I-lqc$, $3-lqc$, $C4c$, $5-lqs$, $Htqa$, $4-Mqc$, Thn , $\alpha-Chpa$,
 Cit , Nua , Pyp and an optionally substituted aromatic α -amino acid,
wherein said optionally substituted aromatic α -amino acid is optionally
20 substituted with one or more substituents selected from the group
consisting of halogen, NO_2 , OH , CN , (C_{1-6}) alkyl, (C_{2-6}) alkenyl, (C_{2-6}) alkynyl,
and NR^9R^{10} ;
 AA^3 is a D- or L-isomer of an amino acid selected from the group consisting
of Cys , $hCys$, Pen , Tpa , and $Tmpa$;

- 63 -

AA^{3b} is the D- or L-isomer of an amino acid selected from the group consisting of R¹¹, Arg, Bpa, F₅-Phe, His, Nal, Pal, 4-Pal, Phe, Trp, hArg, Bip, Tic, , Htic, Dip, Sala, Aala, Thza, Thia, Bal, Fala, Pala, and X⁵-Phe;

AA⁴ is a D- or L-isomer of an amino acid selected from the group consisting of Trp, N-Met-Trp, β -Met-Trp, His, hHis, hArg, Bip, Tic, , Htic, Dip, Sala, Aala, Thza, Thia, Bal, Fala, Pala, and an optionally substituted aromatic α -amino acid;

wherein said optionally substituted aromatic α -amino acid is optionally substituted with one or more substituents each independently selected from the group consisting of halogen, NO₂, OH, CN, (C₁₋₄)alkyl, (C₂₋₄)alkenyl, (C₂₋₄)alkynyl, Bzl, O-Bzl, and NR⁹R¹⁰;

AA⁵ is a D- or L-isomer of an amino acid selected from the group consisting of 4-Pip-Gly, 4-Pip-Ala, *cis*-4-Acha, *trans*-4-Acha, *trans*-4-Amcha, hLys, Lys and Orn, and, hArg, Bip, Tic, , Htic, Dip, Sala, Aala, Thza, Thia, Bal, Fala, Pala,

wherein the side-chain amino group of said amino acid is optionally mono- or di-substituted with R³ and R⁴;

AA⁶ is a D- or L-isomer of an amino acid selected from the group consisting of Cys, hCys, Pen, Tpa, and Tmpa;

AA⁷ is absent or a D- or L-isomer of an amino acid selected from the group consisting of R¹¹, Aic, A3c, A4c, A5c, A6c, Abu, Aib, β -Ala, Arg, Bpa, Cha, Deg, Gaba, His, Ile, Leu, Nal, Nle, Pal, Phe, F₅-Phe, Pro, Sar, Ser, Ser(Bzl), Thr, Thr(Bzl), Trp, N-Me-Trp, Val, N-Me-Val, hArg, Bip, Tic, , Htic, Dip, Sala, Aala, Thza, Thia, Bal, Fala, Pala, and X⁰-Phe;

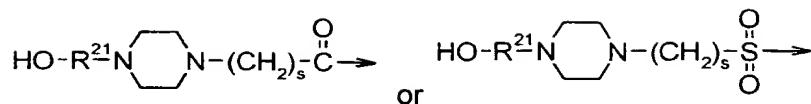
X⁰ is halogen, NO₂, CH₃, OH, CN, Bzl or O-Bzl;

R¹ and R² each is, independently, H, E-, E(O)₂S-, E(O)C-, EOC-, R¹³, or absent;

R⁵ is -OR⁶ or -NR⁷R⁸;

R¹³ is a moiety of the formula

- 64 -



wherein R²¹ is (C₁₋₄)alkyl and s is 1, 2, 3, or 4;

provided that:

at least one of AA¹ or AA² is present;

5 when AA¹ is a D- or L-isomer of Pro, Hyp, Arg, Pip, hArg, Bip, Bpa, Tic, Cmp, , Inc, Inp, Nip, Ppc, Htic, Thi, Tra, Cmpi, Tpr, , Iia, Alla, Aba, Gba, Car, Ipa, Iaa, Inip, Apa, Mim, Thnc, Sala, Aala, Thza, Thia, Bal, Fala, Pala, Dap, Agly, Pgly, Ina, Dipa, Mnf, Inic, I-Iqc, 3-Iqc, C4c, 5-Iqs, Htqa, 4-Mqc, Thn, α -Chpa, Cit, Nua, Pyp or His, AA² cannot be a D- or L-isomer of Pro, Hyp, Arg, Pip, hArg, Bip, Bpa, Tic, Cmp, , Inc, Inp, Nip, Ppc, Htic, Thi, Tra, Cmpi, Tpr, , Iia, Alla, Aba, Gba, Car, Ipa, Iaa, Inip, Apa, Mim, Thnc, Sala, Aala, Thza, Thia, Bal, Fala, Pala, Dap, Agly, Pgly, Ina, Dipa, Mnf, Inic, I-Iqc, 3-Iqc, C4c, 5-Iqs, Htqa, 4-Mqc, Thn, α -Chpa, Cit, Nua, Pyp or His;

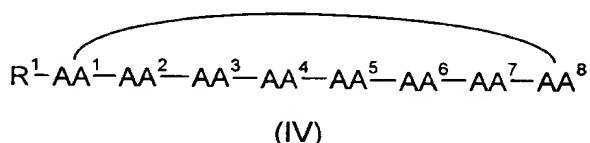
10 when AA⁷ is a D- or L-isomer of Thr or of Ser, AA⁸ cannot be a D- or L-isomer of Thr or of Ser;

15 at least one of AA¹, AA², AA^{3b}, AA⁷, AA^{7b}, or AA⁸ is the D- or L-isomer of R¹¹; and

when one of X² or X³ is =O or =S, the other is absent;

20 or a pharmaceutically acceptable salt thereof.

4. A compound according to claim 1, wherein said compound is of formula (IV):



wherein

- 65 -

AA¹ is absent or the D- or L-isomer of an amino acid selected from the group consisting of R¹¹, Aic, Hyp, Pro, Ser, Ser(Bzl), Thr, Thr(Bzl), Tic, Htic, Fala and an optionally substituted aromatic α -amino acid;

wherein said optionally substituted aromatic α -amino acid is optionally substituted with one or more substituents each independently selected from the group consisting of halogen, NO₂, OH, CN, (C₁₋₆)alkyl, (C₂₋₆)alkenyl, (C₂₋₆)alkynyl, (C₁₋₆)alkoxy, Bzl, O-Bzl, and NR⁹R¹⁰;

AA² is absent or the D- or L-isomer of an amino acid selected from the group consisting of R¹¹, Arg, F₅-Phe, His, Pal, Phe, Trp, hArg, Pala, Bal, Fala, ,

10 Sala and X⁰-Phe;

AA³ is the D- or L-isomer of an optionally substituted aromatic α -amino acid, wherein said optionally substituted aromatic α -amino acid is optionally substituted with one or more substituents selected from the group consisting of halogen, NO₂, OH, CN, (C₁₋₄)alkyl, (C₂₋₄)alkenyl, (C₂₋₄)alkynyl, Bzl, O-Bzl, and NR⁹R¹⁰;

15 AA⁴ is a D- or L-isomer of an optionally substituted amino acid selected from the group consisting of Trp, N-Met-Trp, β -Me-Trp, Lys, Orn, hLys, *cis*-4-Acha, *trans*-4-Acha, *trans*-4-Amcha, 4-Pip-Gly, 4-Pip-Ala, hArg, Bip, Tic, Htic, Dip, Sala, Aala, Thza, Thia, Bal, Fala, and Pala;

20 wherein the side chain amino group of said optionally substituted amino acid is optionally substituted with R³ and R⁴;

AA⁵ is absent or a D- or L-isomer of R¹¹, A3c, A4c, A5c, A6c, Abu, Aib, Aic, β -Ala, Bpa, Cha, Deg, F₅-Phe, Gaba, Ile, Leu, Nal, Nle, Pal, Phe, Pro, Sar, Ser, Ser(Bzl), Thr, Thr(Bzl), Trp, N-Me-Trp, Val, N-Me-Val, hArg, Bip, Tic, ,

25 Htic, Dip, Sala, Aala, Thza, Thia, Bal, Fala, Pala, or X⁰-Phe;

AA⁶ is absent, the D- or L-isomer of R¹¹, an aromatic α -amino acid, F₅-Phe, Phe, Thr, Thr(Bzl), Ser, Ser(Bzl), or X⁰-Phe;

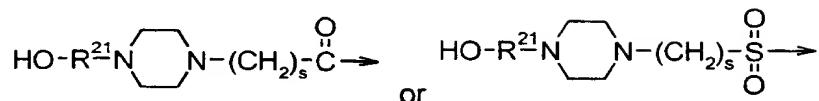
AA⁷ is absent, the D- or L-isomer of R¹¹ or the D- or L-isomer of an aromatic α -amino acid;

- 66 -

AA⁸ is a D- or L- isomer of R¹¹;

R¹ is H, E-, E(O)₂S-, E(O)C-, EOOC-, or R¹³;

R¹³ is a moiety of the formula



5 wherein R²¹ is (C₁₋₄)alkyl and s is 1, 2, 3, or 4;

X⁰ in the definition of AA² and AA⁵ is halogen, NO₂, OH, (C₁₋₆)alkyl, (C₁₋₆)alkoxy, mono- or di-(C₁₋₆)alkylamino, Bzl or O-Bzl;

X⁰ in the definition of AA⁶ is halogen, NO₂, OH, (C₁₋₆)alkyl, (C₁₋₆)alkoxy, mono- or di-(C₁₋₆)alkylamino, Bzl, O-Bzl, or NR⁹R¹⁰;

10 provided that:

at least one of AA¹ or AA² is present;

when AA¹ is absent, AA² and AA⁸ together form a bond; and

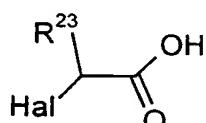
at least two of AA⁵, AA⁶, and AA⁷ are present;

or a pharmaceutically acceptable salt thereof.

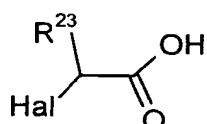
15

5. A compound according to claim 2, wherein

AA¹ is absent, Ac-D-Phe, or the D- or L- isomer of R¹¹, Pip, Pro, or Ser, or of an aromatic α -amino acid selected from the group consisting of Cpa, Dip, Nal, Pal, and Phe;



20 AA² is absent, Aic, Pal, Phe, F₅-Phe, 4-NO₂-Phe, Trp, Tyr, Phe(4-O-Bzl)



AA³ is the D- or L- isomer of an amino acid selected from the group consisting of Pen, Cys, hCys and Tmpa;

AA⁴ is the D- or L-isomer of Trp, His, N-Me-Trp, β -Me-Trp, hTrp, or hHis;

AA⁵ is Lys, hLys, N-Me-Lys, Orn, cis-4-Acha or 4-Pip-Ala;

5 AA⁶ is the D- or L-isomer of an amino acid selected from the group consisting of Cys, hCys, Pen and Tmpa;

AA⁷ is A3c, A4c, A5c, A6c, Abu, Aic, β -Ala, Gaba, Nle, F₅-Phe, Phe, Pro, Sar, Ser, Thr, Thr(Bzl), Tyr, Val or absent; and

AA⁸ is R¹¹, Nal, Thr, Thr(Bzl), Tyr, Phe(4-O-Bzl), or absent;

10 or a pharmaceutically acceptable salt thereof.

6. A compound according to claim 5, wherein

AA¹ is absent or the D- or L- isomer of R¹¹, Pip or Pro, or of an aromatic α -amino acid selected from the group consisting of Cpa, Dip, Nal, Pal, Phe, and Ac-Phe;

15 AA² is Tyr, Pal, Phe, 4-NO₂-Phe, Trp, or absent;

AA³ is a D- or L-isomer of Cys or Pen;

AA⁴ is D-Trp;

AA⁵ is Lys, Orn, or cis-4-Acha;

20 AA⁶ is a D- or L-isomer of Cys or Pen;

AA⁷ is A3c, A4c, A5c, A6c, Abu, Aic, β -Ala, Gaba, Nle, Phe, Pro, Sar, Thr, Thr(Bzl), Tyr, Val, or absent; and

AA⁸ is R¹¹, Thr, Tyr, Nal, or absent;

or a pharmaceutically acceptable salt thereof.

25

7. A compound according to claim 3, wherein

AA¹ is R¹¹, Aic, Hca, Pro, Ser, Ser(Bzl), Trp, Tyr, or a D- or L-isomer of an aromatic α -amino acid selected from the group consisting of Cpa, Nal, Ac-Nal, Phe, Ac-Phe, 4-NO₂-Phe, and Ac-4-NO₂-Phe;

- 68 -

AA² is Pal, Phe, F₅-Phe, Tyr, or absent;

AA³ is a D- or L-isomer of Cys, hCys, Pen or Tmpa;

AA^{3b} is Pal, 4-Pal, His, Trp, Tyr, Phe(4-O-Bzl), Phe, or R¹¹;

AA⁴ is a D- or L-isomer of Trp or His;

5 AA⁵ is Lys, N-Me-Lys, Orn, hLys, cis-4-Acha, or 4-Pip-Ala;

AA⁶ is a D- or L-isomer of Cys, hCys, Pen or Tmpa;

AA⁷ is R¹¹, A4c, A5c, Abu, β -Ala, Gaba, Phe, F₅-Phe, Ser(Bzl), Thr, Thr(Bzl), Phe(4-O-Bzl), or absent;

AA^{7b} is R¹¹, Nal, F₅-Phe, X⁰-Phe or absent, wherein X⁰ is halogen, NO₂, CH₃,

10 OH, Bzl or O-Bzl; and

AA⁸ is R¹¹, Nal, Tyr, Phe(4-O-Bzl), or absent;

or a pharmaceutically acceptable salt thereof.

8. A compound according to claim 7, wherein

15 AA¹ is R¹¹, Aic, Hca, Pro, Ser(Bzl), or a D- or L-isomer of an aromatic α -amino acid selected from the group consisting of Cpa, Nal, Ac-Nal, Phe, Ac-Phe, 4-NO₂-Phe, and Ac-4-NO₂-Phe;

AA² is Pal, Tyr, or absent;

AA³ is a D- or L-isomer of Cys or Pen;

20 AA^{3b} is R¹¹, Pal, 4-Pal, Trp, Tyr, Phe(4-O-Bzl), or Phe, wherein R¹¹ is (T)aeg;

AA⁴ is D-Trp;

AA⁵ is Lys, N-Me-Lys, Orn, or cis-4-Acha;

AA⁶ is a D- or L-isomer of Cys or Pen;

AA⁷ is R¹¹, A5c, Abu, Ser(Bzl), Thr, Thr(Bzl), Phe(4-O-Bzl), Gaba, or absent;

25 AA^{7b} is Nal, X⁰-Phe or absent; and

AA⁸ is Tyr or absent;

or a pharmaceutically acceptable salt thereof.

9. A compound according to claim 4, wherein

- 69 -

AA¹ is Aic, Hyp, Cpa, D-Cpa, Nal, Pal, Phe, Pro, R¹¹, Tyr or absent;
AA² is Phe, Trp, F₅-Phe, His, Tyr, Phe(4-O-Bzl), or R¹¹;
AA³ is a D-isomer of Trp, His, or Pal;
AA⁴ is Lys, N-Me-Lys, Orn, hLys, cis-4-Acha, or 4-Pip-Ala;
5 AA⁵ is Pal, Phe(4-O-Bzl), Thr(Bzl), Thr, Sar, Gaba, β -Ala, A4c, A5c, A6c, Abu, Aic or absent;
AA⁶ is Thr, Tyr, Ser, F₅-Phe, Cpa, Nal, or D- or L-Phe;
AA⁷ is Nal, Pal, or absent; and
AA⁸ is R¹¹;
10 or a pharmaceutically acceptable salt thereof.

10. A compound according to claim 9, wherein
AA¹ is Cpa, Nal, Pal, Phe, Tyr or absent;
AA² is Phe, Tyr, Trp, or R¹¹;
15 AA³ is D-Trp;
AA⁴ is Lys, N-Me-Lys, or cis-4-Acha;
AA⁵ is Pal, Phe(4-O-Bzl), Aic, Gaba, A5c or absent;
AA⁶ is Thr, Nal, or D- or L-Phe;
AA⁷ is absent; and
20 AA⁸ is R¹¹;
or a pharmaceutically acceptable salt thereof.

11. A compound according to claim 2, wherein R¹ and R⁵ are absent
and the N-terminal amino acid and the C-terminal amino acid together form
25 an amide bond; or a pharmaceutically acceptable salt thereof.

12. A compound according to claim 3, wherein R¹ and R⁵ are absent
and the N-terminal amino acid and the C-terminal amino acid together form
an amide bond; or a pharmaceutically acceptable salt thereof.

- 70 -

13. A compound according to claim 6, wherein said compound is of the formula:

5 Ac-D-Phe-Tyr-cyclo(D-Cys-D-Trp-Lys-Cys)-Abu-Thr-NH₂;
 Nal-Tyr-cyclo(Cys-D-Trp-Lys-D-Cys)-Val-Nal-NH₂;
 Nal-Tyr-cyclo(Cys-D-Trp-Lys-D-Cys)-Abu-Nal-NH₂;
 D-Dip-Tyr-cyclo(Cys-D-Trp-Lys-D-Cys)-Abu-Nal-NH₂;
 Dip-Tyr-cyclo(D-Cys-D-Trp-Lys-D-Cys)-Abu-Nal-NH₂;
 Nal-Tyr-cyclo(D-Cys-D-Trp-Lys-D-Cys)-Abu-Nal-NH₂;
10 Dip-Tyr-cyclo(D-Cys-D-Trp-Lys-D-Cys)-Val-Nal-NH₂;
 Nal-Tyr-cyclo(D-Cys-D-Trp-Lys-D-Cys)-Val-Nal-NH₂;
 cyclo(D-Phe-Tyr-cyclo(D-Cys-D-Trp-Lys-Cys)-Abu-Thr);
 Cpa-Pal-cyclo(D-Cys-D-Trp-Lys-D-Cys)-A3c-Nal-NH₂;
 Cpa-Pal-cyclo(D-Cys-D-Trp-Lys-D-Cys)-A5c-Nal-NH₂;
15 Cpa-Pal-cyclo(D-Cys-D-Trp-Lys-D-Cys)-A6c-Nal-NH₂;
 (G(z))aeg-cyclo(D-Cys-D-Trp-Lys-D-Cys)-A5c-Nal-NH₂;
 Pal-cyclo(D-Cys-D-Trp-Lys-D-Cys)-A5c-Nal-NH₂;
 Cpa-Pal-cyclo(D-Cys-D-Trp-Lys-D-Cys)- β -Ala-Nal-NH₂;
 Cpa-Pal-cyclo(D-Cys-D-Trp-Lys-D-Cys)-Sar-Nal-NH₂;
20 Cpa-Pal-cyclo(D-Cys-D-Trp-Lys-D-Cys)-Gaba-Nal-NH₂;
 Cpa-Pal-cyclo(D-Cys-D-Trp-Lys-D-Cys)-Pro-Nal-NH₂;
 Pro-Phe-c(D-Cys-D-Trp-Lys-D-Cys)-Nle-Phe-NH₂;
 Pro-Phe-c(D-Cys-D-Trp-Lys-D-Cys)-Thr-Nle-NH₂;
 Pro-Phe-c(D-Cys-D-Trp-Lys-D-Cys)-Thr-Phe-NH₂;
25 Cpa-Phe-c(D-Cys-D-Trp-Lys-D-Cys)-Gaba-NH₂;
 Cpa-Phe-c(D-Cys-D-Trp-Lys-D-Cys)-Gaba-Tyr-NH₂;
 Pip-Phe-c(D-Cys-D-Trp-Lys-D-Cys)-NH₂;
 Pip-Phe-c(Cys-D-Trp-Lys-Cys)-Gaba-NH₂; or
 Pro-Phe-c(D-Cys-D-Trp-Lys-D-Cys)-Thr-NH₂;

- 71 -

or a pharmaceutically acceptable salt thereof.

14. A compound according to claim 6, wherein said compound is according to the formula:

5 Phe-cyclo(Cys-D-Trp-Lys-Cys)-Thr-NH₂;
 Phe-Tyr-cyclo(D-Cys-D-Trp-Lys-Cys)-Abu-Thr-NH₂;
 Ac-D-Phe-Tyr-cyclo(D-Cys-D-Trp-Lys-Cys)-Abu-Thr-NH₂;
 Nal-Tyr-cyclo(Cys-D-Trp-Lys-D-Cys)-Val-Nal-NH₂;
 Nal-Tyr-cyclo(Cys-D-Trp-Lys-D-Cys)-Abu-Nal-NH₂;

10 Dip-Tyr-cyclo(D-Cys-D-Trp-Lys-D-Cys)-Abu-Nal-NH₂;
 Nal-Tyr-cyclo(D-Cys-D-Trp-Lys-D-Cys)-Abu-Nal-NH₂;
 Dip-Tyr-cyclo(D-Cys-D-Trp-Lys-D-Cys)-Val-Nal-NH₂;
 Nal-Tyr-cyclo(D-Cys-D-Trp-Lys-D-Cys)-Val-Nal-NH₂;
 Cpa-Pal-cyclo(D-Cys-D-Trp-Lys-D-Cys)-A3c-Nal-NH₂;

15 Cpa-Pal-cyclo(D-Cys-D-Trp-Lys-D-Cys)-A5c-Nal-NH₂;
 Cpa-Pal-cyclo(D-Cys-D-Trp-Lys-D-Cys)-A6c-Nal-NH₂;
 (G(z))aeg-cyclo(D-Cys-D-Trp-Lys-D-Cys)-A5c-Nal-NH₂;
 D-Cpa-cyclo(Cys-D-Trp-Lys-D-Cys)-A5c-Nal-NH₂;
 Pal-cyclo(D-Cys-D-Trp-Lys-D-Cys)-A5c-Nal-NH₂;

20 Cpa-cyclo(D-Cys-D-Trp-Lys-D-Cys)-A5c-Nal-NH₂;
 Cpa-Pal-cyclo(D-Cys-D-Trp-Lys-D-Cys)- β -Ala-Nal-NH₂;
 Cpa-Pal-cyclo(D-Cys-D-Trp-Lys-D-Cys)-Sar-Nal-NH₂;
 Cpa-Pal-cyclo(D-Cys-D-Trp-Lys-D-Cys)-Aic-Nal-NH₂;
 Cpa-Pal-cyclo(D-Cys-D-Trp-Lys-D-Cys)-Gaba-Nal-NH₂;

25 Cpa-Pal-cyclo(D-Cys-D-Trp-Lys-D-Cys)-Pro-Nal-NH₂;
 (T)aeg-cyclo(D-Cys-D-Trp-Lys-D-Cys)-(A)aeg-NH₂;
 Cpa-Pal-cyclo(D-Cys-D-Trp-Lys-D-Cys)-A4c-Nal-NH₂;
 Cpa-Pal-cyclo(D-Cys-D-Trp-Lys-D-Cys)-Nal-NH₂;
 Pal-cyclo(D-Cys-D-Trp-Lys-D-Cys)-Nal-NH₂;

- 72 -

Pro-Phe-cyclo(Cys-D-Trp-Lys-D-Cys)-Val-NH₂;
Pro-Phe-cyclo(D-Cys-D-Trp-Lys-Cys)-Val-NH₂;
Pip-4-NO₂-Phe-cyclo(D-Cys-D-Trp-Lys-D-Cys)-Nle-NH₂;
(G)aeg-Pal-cyclo(D-Cys-D-Trp-Lys-D-Cys)-Thr(Bzl)-(C)aeg-NH₂; or
5 (C)aeg-Pal-cyclo(D-Cys-D-Trp-Lys-D-Cys)-Thr(Bzl)-(G)aeg-NH₂;
or a pharmaceutically acceptable salt thereof.

15. A compound according to claim 8, wherein said compound is according to the formula

10 Nal-cyclo(D-Cys-Tyr-D-Trp-Lys-Cys)-Nal-NH₂;
D-Nal-cyclo(D-Cys-Tyr-D-Trp-Lys-Cys)-Nal-NH₂;
D-Phe-cyclo(Cys-Tyr-D-Trp-Lys-Cys)-Thr-NH₂;
D-4-NO₂-Phe-cyclo(D-Cys-Tyr-D-Trp-Lys-Cys)-Nal-NH₂;
Ac-D-4-NO₂-Phe-cyclo(D-Cys-Tyr-D-Trp-Lys-Cys)-Nal-NH₂;
15 D-4-NO₂-Phe-Pal-cyclo(D-Cys-Phe(4-O-Bzl)-D-Trp-Lys-Cys)-Tyr-NH₂;
Cpa-cyclo(D-Cys-Pal-D-Trp-Lys-Cys)-Thr(Bzl)-Tyr-NH₂;
D-4-NO₂-Phe-cyclo(D-Cys-Pal-D-Trp-Lys-Cys)-Thr-Tyr-NH₂;
D-4-NO₂-Phe-cyclo(D-Cys-Pal-D-Trp-Lys-Cys)-Thr(Bzl)-NH₂;
D-4-NO₂-Phe-cyclo(D-Cys-Pal-D-Trp-Lys-D-Cys)-Thr(Bzl)-Tyr-NH₂;
20 D-4-NO₂-Phe-cyclo(D-Cys-Tyr-D-Trp-Lys-Cys)-Thr(Bzl)-Tyr-NH₂;
4-NO₂-Phe-cyclo(D-Cys-Pal-D-Trp-Lys-Cys)-Thr(Bzl)-Tyr-NH₂;
D-Nal-cyclo(D-Cys-Pal-D-Trp-Lys-Cys)-Thr(Bzl)-Tyr-NH₂;
Pro-cyclo(D-Cys-Pal-D-Trp-Lys-Cys)-Thr(Bzl)-Tyr-NH₂;
25 Cpa-cyclo(D-Cys-Pal-D-Trp-Lys-Cys)-Thr(Bzl)-Nal-NH₂;
Ser(Bzl)-cyclo(D-Cys-Pal-D-Trp-Lys-Cys)-Thr-Tyr-NH₂;
(T)aeg-cyclo(D-Cys-Pal-D-Trp-Lys-D-Cys)-Thr(Bzl)-Tyr-NH₂;
(A)aeg-cyclo(D-Cys-Pal-D-Trp-Lys-Cys)-Thr(Bzl)-Tyr-NH₂;
(G)aeg-cyclo(D-Cys-Pal-D-Trp-Lys-Cys)-Thr(Bzl)-Tyr-NH₂;
(T)aeg-cyclo(D-Cys-4-Pal-D-Trp-Lys-Cys)-Thr(Bzl)-Tyr-NH₂;

- 73 -

(T)aeg-cyclo(D-Cys-Tyr-D-Trp-Lys-Cys)-Thr(Bzl)-Tyr-NH₂;
(T)aeg-cyclo(D-Cys-Phe-D-Trp-Lys-Cys)-Thr(Bzl)-Tyr-NH₂;
(T)aeg-cyclo(D-Cys-(T)aeg-D-Trp-Lys-Cys)-Thr(Bzl)-Tyr-NH₂;
(T)aeg-cyclo(D-Cys-Pal-D-Trp-Lys-Cys)-Ser(Bzl)-Tyr-NH₂;
5 (T)aeg-cyclo(D-Cys-Pal-D-Trp-Lys-Cys)-Phe(4-O-Bzl)-Tyr-NH₂;
(T)aeg-cyclo(D-Cys-Pal-D-Trp-Lys-Cys)-A5c-Tyr-NH₂;
(T)aeg-cyclo(D-Cys-Pal-D-Trp-Lys-Cys)-Abu-Tyr-NH₂;
D-Cpa-cyclo(D-Cys-(T)aeg-D-Trp-Lys-Cys)-Thr(Bzl)-Tyr-NH₂;
10 (C)aeg-c(D-Cys-Pal-D-Trp-Lys-D-Cys)-Thr(Bzl)-Tyr-NH₂;
D-Cpa-c(D-Cys-Pal-D-Trp-Lys-D-Cys)-Thr(Bzl)-Tyr-NH₂;
(T)aeg-c(Pen-Pal-D-Trp-Lys-D-Cys)-Thr(Bzl)-Tyr-NH₂;
(T)aeg-c(D-Cys-Trp-D-Trp-Lys-D-Cys)-Thr(Bzl)-Tyr-NH₂;
(T)aeg-c(D-Cys-Phe-D-Trp-Lys-D-Cys)-Thr(Bzl)-Tyr-NH₂;
15 (T)aeg-c(D-Cys-Pal-D-Trp-Orn-D-Cys)-Thr(Bzl)-Tyr-NH₂;
(T)aeg-c(D-Cys-Pal-D-Trp-hLys-D-Cys)-Thr(Bzl)-Tyr-NH₂;
(T)aeg-c(D-Cys-Pal-D-Trp-Iamp-D-Cys)-Thr(Bzl)-Tyr-NH₂;
(T)aeg-c(D-Cys-Pal-D-Trp-Cha(4-am)-D-Cys)-Thr(Bzl)-Tyr-NH₂;
(T)aeg-c(D-Cys-Pal-D-Trp-Lys-D-Cys)-Ser(Bzl)-Tyr-NH₂;
20 (T)aeg-c(D-Cys-Pal-D-Trp-Lys-D-Cys)-Thr(Bzl)-D-Tyr-NH₂;
(T)aeg-c(D-Cys-Pal-D-Trp-Lys-D-Cys)-Thr(Bzl)-Trp-NH₂;
(T)aeg-c(D-Cys-Pal-D-Trp-Lys-D-Pen)-Thr(Bzl)-Tyr-NH₂;
(C)aeg-c(D-Cys-Phe-D-Trp-Lys-D-Cys)-Thr(Bzl)-Tyr-NH₂;
Ina-c(D-Cys-Phe-D-Trp-Lys-D-Cys)-Thr(Bzl)-Tyr-NH₂;
Mnf-c(D-Cys-Phe-D-Trp-Lys-D-Cys)-Thr(Bzl)-Tyr-NH₂;
25 Inp-c(D-Cys-Phe-D-Trp-Lys-D-Cys)-Thr(Bzl)-Tyr-NH₂;
Nua-c(D-Cys-Phe-D-Trp-Lys-D-Cys)-Thr(Bzl)-Tyr-NH₂;
(T)aeg-Pal-c(D-Cys-D-Trp-Lys-D-Cys)-Thr(Bzl)-Tyr-NH₂;
(T)aeg-Pal-c(D-Cys-D-Trp-Lys-D-Cys)-Tyr(Bzl)-Thr-NH₂;
(C)aeg-Phe-c(D-Cys-D-Trp-Lys-D-Cys)-Thr(Bzl)-Tyr-NH₂; or

- 74 -

(T)aeg-D-Trp-c(D-Cys-Pal-Lys-D-Cys)Thr(Bzl)-Leu-NH₂;
or a pharmaceutically acceptable salt thereof.

16. A compound according to claim 8, wherein said compound is
5 according to the formula

Hca-cyclo(D-Cys-Tyr-D-Trp-Lys-Cys)-Nal-NH₂;
Ac-Nal-cyclo(D-Cys-Tyr-D-Trp-Lys-Cys)-Nal-NH₂;
Ac-D-Phe-cyclo(D-Cys-Tyr-D-Trp-Lys-Cys)-Nal-NH₂;
Ac-D-Nal-cyclo(D-Cys-Tyr-D-Trp-Lys-Cys)-Nal-NH₂;
10 D-Phe-cyclo(D-Cys-Tyr-D-Trp-Lys-Cys)-Nal-NH₂;
Nal-cyclo(D-Cys-Tyr-D-Trp-Lys-Cys)-Nal-NH₂;
D-Nal-cyclo(D-Cys-Tyr-D-Trp-Lys-Cys)-Nal-NH₂;
D-Phe-cyclo(Cys-Tyr-D-Trp-Lys-Cys)-Thr-NH₂;
D-4-NO₂-Phe-cyclo(D-Cys-Tyr-D-Trp-Lys-Cys)-Nal-NH₂;
15 Ac-D-4-NO₂-Phe-cyclo(D-Cys-Tyr-D-Trp-Lys-Cys)-Nal-NH₂;
D-4-NO₂-Phe-Pal-cyclo(D-Cys-Phe(4-O-Bzl)-D-Trp-Lys-Cys)-Tyr-NH₂;
D-4-NO₂-Phe-cyclo(D-Cys-Pal-D-Trp-Lys-Cys)-Thr(Bzl)-Tyr-NH₂;
Cpa-cyclo(D-Cys-Pal-D-Trp-Lys-Cys)-Thr(Bzl)-Tyr-NH₂;
D-4-NO₂-Phe-cyclo(D-Cys-Pal-D-Trp-Lys-Cys)-Thr(Bzl)-NH₂;
20 D-4-NO₂-Phe-cyclo(D-Cys-Pal-D-Trp-Lys-D-Cys)-Thr(Bzl)-Tyr-NH₂;
D-4-NO₂-Phe-cyclo(D-Cys-Tyr-D-Trp-Lys-Cys)-Thr(Bzl)-Tyr-NH₂;
4-NO₂-Phe-cyclo(D-Cys-Pal-D-Trp-Lys-Cys)-Thr(Bzl)-Tyr-NH₂;
D-Nal-cyclo(D-Cys-Pal-D-Trp-Lys-Cys)-Thr(Bzl)-Tyr-NH₂;
Pro-cyclo(D-Cys-Pal-D-Trp-Lys-Cys)-Thr(Bzl)-Tyr-NH₂;
25 Cpa-cyclo(D-Cys-Pal-D-Trp-Lys-Cys)-Thr(Bzl)-Nal-NH₂;
Ser(Bzl)-cyclo(D-Cys-Pal-D-Trp-Lys-Cys)-Thr-Tyr-NH₂;
(T)aeg-cyclo(D-Cys-Pal-D-Trp-Lys-Cys)-Thr(Bzl)-Tyr-NH₂;
(C)aeg-cyclo(D-Cys-Pal-D-Trp-Lys-Cys)-Thr(Bzl)-Tyr-NH₂;
Aic-cyclo(D-Cys-Pal-D-Trp-Lys-Cys)-Thr(Bzl)-Tyr-NH₂;

- 75 -

(C(z))aeg-cyclo(D-Cys-Pal-D-Trp-Lys-Cys)-Thr(Bzl)-Tyr-NH₂;
(A(z))aeg-cyclo(D-Cys-Pal-D-Trp-Lys-Cys)-Thr(Bzl)-Tyr-NH₂;
(T)aeg-cyclo(D-Cys-Pal-D-Trp-Lys-D-Cys)-Thr(Bzl)-Tyr-NH₂;
(A)aeg-cyclo(D-Cys-Pal-D-Trp-Lys-Cys)-Thr(Bzl)-Tyr-NH₂;
5 (G)aeg-cyclo(D-Cys-Pal-D-Trp-Lys-Cys)-Thr(Bzl)-Tyr-NH₂;
(T)aeg-cyclo(D-Cys-4-Pal-D-Trp-Lys-Cys)-Thr(Bzl)-Tyr-NH₂;
(T)aeg-cyclo(D-Cys-Tyr-D-Trp-Lys-Cys)-Thr(Bzl)-Tyr-NH₂;
(T)aeg-cyclo(D-Cys-Phe-D-Trp-Lys-Cys)-Thr(Bzl)-Tyr-NH₂;
(T)aeg-cyclo(D-Cys-(T)aeg-D-Trp-Lys-Cys)-Thr(Bzl)-Tyr-NH₂;
10 (T)aeg-cyclo(D-Cys-Pal-D-Trp-Lys-Cys)-Ser(Bzl)-Tyr-NH₂;
(T)aeg-cyclo(D-Cys-Pal-D-Trp-Lys-Cys)-Phe(4-O-Bzl)-Tyr-NH₂;
(T)aeg-cyclo(D-Cys-Pal-D-Trp-Lys-Cys)-A5c-Tyr-NH₂;
(T)aeg-cyclo(D-Cys-Pal-D-Trp-Lys-Cys)-Abu-Tyr-NH₂;
D-Cpa-cyclo(D-Cys-(T)aeg-D-Trp-Lys-Cys)-Thr(Bzl)-Tyr-NH₂;
15 (T)aeg-cyclo(D-Cys-Pal-D-Trp-Lys-D-Cys)-Thr(Bzl)-p-Me-Phe-NH₂;
Ac-(T)aeg-cyclo(D-Cys-Pal-D-Trp-Lys-D-Cys)-Thr(Bzl)-Tyr-NH₂;
(T)aeg-cyclo(D-Cys-Pal-D-Trp-Lys-D-Cys)-Nal-NH₂;
D-Cpa-cyclo(D-Cys-Pal-D-Trp-Lys-D-Cys)-Nal-NH₂;
(A)aeg-cyclo(D-Cys-Pal-D-Trp-Lys-D-Cys)-Thr(Bzl)-Tyr-NH₂; (C)aeg-
20 cyclo(D-Cys-Pal-D-Trp-Lys-D-Cys)-Thr(Bzl)-Tyr-NH₂;
(C)aeg-c(D-Cys-Pal-D-Trp-Lys-D-Cys)-Thr(Bzl)-Tyr-NH₂;
D-Cpa-c(D-Cys-Pal-D-Trp-Lys-D-Cys)Thr(Bzl)-Tyr-NH₂;
(T)aeg-c(Pen-Pal-D-Trp-Lys-D-Cys)Thr(Bzl)-Tyr-NH₂;
(T)aeg-c(D-Cys-Trp-D-Trp-Lys-D-Cys)Thr(Bzl)-Tyr-NH₂;
25 (T)aeg-c(D-Cys-Phe-D-Trp-Lys-D-Cys)Thr(Bzl)-Tyr-NH₂;
(T)aeg-c(D-Cys-Pal-D-Trp-Orn-D-Cys)Thr(Bzl)-Tyr-NH₂;
(T)aeg-c(D-Cys-Pal-D-Trp-hLys-D-Cys)Thr(Bzl)-Tyr-NH₂;
(T)aeg-c(D-Cys-Pal-D-Trp-lamp-D-Cys)Thr(Bzl)-Tyr-NH₂;
(T)aeg-c(D-Cys-Pal-D-Trp-Cha(4-am)-D-Cys)Thr(Bzl)-Tyr-NH₂;

- 76 -

(T)aeg-c(D-Cys-Pal-D-Trp-Lys-D-Cys)-Ser(Bzl)-Tyr-NH₂;
(T)aeg-c(D-Cys-Pal-D-Trp-Lys-D-Cys)Thr(Bzl)-D-Tyr-NH₂;
(T)aeg-c(D-Cys-Pal-D-Trp-Lys-D-Cys)Thr(Bzl)-Trp-NH₂;
(T)aeg-c(D-Cys-Pal-D-Trp-Lys-D-Pen)Thr(Bzl)-Tyr-NH₂;
5 (C)aeg-c(D-Cys-Phe-D-Trp-Lys-D-Cys)Thr(Bzl)-Tyr-NH₂;
Ina-c(D-Cys-Phe-D-Trp-Lys-D-Cys)-Thr(Bzl)-Tyr-NH₂;
Mnf-c(D-Cys-Phe-D-Trp-Lys-D-Cys)-Thr(Bzl)-Tyr-NH₂;
Inp-c(D-Cys-Phe-D-Trp-Lys-D-Cys)-Thr(Bzl)-Tyr-NH₂;
Nua-c(D-Cys-Phe-D-Trp-Lys-D-Cys)-Thr(Bzl)-Tyr-NH₂;
10 (T)aeg-Pal-c(D-Cys-D-Trp-Lys-D-Cys)Thr(Bzl)-Tyr-NH₂;
(T)aeg-Pal-c(D-Cys-D-Trp-Lys-D-Cys)Tyr(Bzl)-Thr-NH₂;
(C)aeg-Phe-c(D-Cys-D-Trp-Lys-D-Cys)Thr(Bzl)-Tyr-NH₂; or
(T)aeg-D-Trp-c(D-Cys-Pal-Lys-D-Cys)Thr(Bzl)-Leu-NH₂;
or a pharmaceutically acceptable salt thereof.

15 17. A compound according to claim 10, wherein said compound is
according to the formula

cyclo(Trp-D-Trp-Lys-Phe(4-O-Bzl)-Phe-(T)aeg);
cyclo(Trp-D-Trp-Lys-Pal-Phe -(T)aeg); or
20 cyclo(Phe-Phe-D-Trp-Lys-Thr-(T)aeg);
or a pharmaceutically acceptable salt thereof.

18. A method of eliciting a neuromedin B receptor agonist effect in a
subject in need thereof, wherein said method comprises administering to
25 said subject an effective amount of a compound according to claim 13 or a
pharmaceutically acceptable salt thereof.

19. A method of eliciting a somatostatin receptor agonist effect in a
subject in need thereof, wherein said method comprises administering to

said subject an effective amount of a compound according to claim 14 or a pharmaceutically acceptable salt thereof.

20. A method of eliciting a neuromedin B receptor agonist effect in a
5 subject in need thereof, wherein said method comprises administering to
said subject an effective amount of a compound according to claim 15 or a
pharmaceutically acceptable salt thereof.

21. A method of eliciting a somatostatin receptor agonist effect in a
10 subject in need thereof, wherein said method comprises administering to
said subject an effective amount of a compound according to claim 16 or a
pharmaceutically acceptable salt thereof.

22. A method of eliciting a somatostatin receptor agonist effect in a
15 subject in need thereof, wherein said method comprises administering to
said subject an effective amount of a compound according to claim 17 or a
pharmaceutically acceptable salt thereof, provided said compound is not
cyclo(Trp-D-Trp-Lys-Phe(4-O-Bzl)-Phe-(T)aeg); or
cyclo(Trp-D-Trp-Lys-Pal-Phe -(T)aeg).

20
23. A method of eliciting a SSTR-1 agonist effect in a subject in need
thereof, wherein said method comprises administering to said subject an
effective amount of a compound according to claim 14 or a pharmaceutically
acceptable salt thereof, provided said compound is not

25 Nal-Tyr-cyclo(Cys-D-Trp-Lys-D-Cys)-Val-Nal-NH₂;
Nal-Tyr-cyclo(Cys-D-Trp-Lys-D-Cys)-Abu-Nal-NH₂;
Dip-Tyr-cyclo(D-Cys-D-Trp-Lys-D-Cys)-Abu-Nal-NH₂;
Nal-Tyr-cyclo(D-Cys-D-Trp-Lys-D-Cys)-Abu-Nal-NH₂;
Dip-Tyr-cyclo(D-Cys-D-Trp-Lys-D-Cys)-Val-Nal-NH₂;

- 78 -

Nal-Tyr-cyclo(D-Cys-D-Trp-Lys-D-Cys)-Val-Nal-NH₂;
Cpa-Pal-cyclo(D-Cys-D-Trp-Lys-D-Cys)-A3c-Nal-NH₂;
Cpa-Pal-cyclo(D-Cys-D-Trp-Lys-D-Cys)-A5c-Nal-NH₂;
Cpa-Pal-cyclo(D-Cys-D-Trp-Lys-D-Cys)-A6c-Nal-NH₂;
5 (G(z))aeg-cyclo(D-Cys-D-Trp-Lys-D-Cys)-A5c-Nal-NH₂;
D-Cpa-cyclo(Cys-D-Trp-Lys-D-Cys)-A5c-Nal-NH₂;
Pal-cyclo(D-Cys-D-Trp-Lys-D-Cys)-A5c-Nal-NH₂;
Cpa-cyclo(D-Cys-D-Trp-Lys-D-Cys)-A5c-Nal-NH₂;
Cpa-Pal-cyclo(D-Cys-D-Trp-Lys-D-Cys)- β -Ala-Nal-NH₂;
10 cyclo(D-Cys-D-Trp-Lys-D-Cys)-A5c-Nal-NH₂;
Cpa-Pal-cyclo(D-Cys-D-Trp-Lys-D-Cys)-Sar-Nal-NH₂;
Cpa-Pal-cyclo(D-Cys-D-Trp-Lys-D-Cys)-Aic-Nal-NH₂;
Cpa-Pal-cyclo(D-Cys-D-Trp-Lys-D-Cys)-Gaba-Nal-NH₂; or
Cpa-Pal-cyclo(D-Cys-D-Trp-Lys-D-Cys)-Pro-Nal-NH₂.
15
24. A method of eliciting a SSTR-1 agonist effect in a subject in need thereof, wherein said method comprises administering to said subject an effective amount of a compound according to claim 16 or a pharmaceutically acceptable salt thereof provided said compound is not
20 Ac-D-Phe-cyclo(D-Cys-Tyr-D-Trp-Lys-Cys)-Nal-NH₂;
Ac-D-Nal-cyclo(D-Cys-Tyr-D-Trp-Lys-Cys)-Nal-NH₂;
D-Phe-cyclo(D-Cys-Tyr-D-Trp-Lys-Cys)-Nal-NH₂;
Nal-cyclo(D-Cys-Tyr-D-Trp-Lys-Cys)-Nal-NH₂;
D-Nal-cyclo(D-Cys-Tyr-D-Trp-Lys-Cys)-Nal-NH₂;
25 D-4-NO₂-Phe-cyclo(D-Cys-Pal-D-Trp-Lys-Cys)-Thr(Bzl)-Tyr-NH₂;
Cpa-cyclo(D-Cys-Pal-D-Trp-Lys-Cys)-Thr(Bzl)-Tyr-NH₂;
D-4-NO₂-Phe-cyclo(D-Cys-Pal-D-Trp-Lys-Cys)-Thr(Bzl)-NH₂;
D-4-NO₂-Phe-cyclo(D-Cys-Pal-D-Trp-Lys-D-Cys)-Thr(Bzl)-Tyr-NH₂;
D-4-NO₂-Phe-cyclo(D-Cys-Tyr-D-Trp-Lys-Cys)-Thr(Bzl)-Tyr-NH₂;

- 79 -

4-NO₂-Phe-cyclo(D-Cys-Pal-D-Trp-Lys-Cys)-Thr(Bzl)-Tyr-NH₂;
D-Nal-cyclo(D-Cys-Pal-D-Trp-Lys-Cys)-Thr(Bzl)-Tyr-NH₂;
Pro-cyclo(D-Cys-Pal-D-Trp-Lys-Cys)-Thr(Bzl)-Tyr-NH₂;
Cpa-cyclo(D-Cys-Pal-D-Trp-Lys-Cys)-Thr(Bzl)-Nal-NH₂;
5 Ser(Bzl)-cyclo(D-Cys-Pal-D-Trp-Lys-Cys)-Thr-Tyr-NH₂;
(T)aeg-cyclo(D-Cys-Pal-D-Trp-Lys-Cys)-Thr(Bzl)-Tyr-NH₂;
(C)aeg-cyclo(D-Cys-Pal-D-Trp-Lys-Cys)-Thr(Bzl)-Tyr-NH₂;
Aic-cyclo(D-Cys-Pal-D-Trp-Lys-Cys)-Thr(Bzl)-Tyr-NH₂;
(T)aeg-cyclo(D-Cys-Pal-D-Trp-Lys-D-Cys)-Thr(Bzl)-Tyr-NH₂;
10 (A)aeg-cyclo(D-Cys-Pal-D-Trp-Lys-Cys)-Thr(Bzl)-Tyr-NH₂;
(G)aeg-cyclo(D-Cys-Pal-D-Trp-Lys-Cys)-Thr(Bzl)-Tyr-NH₂;
(T)aeg-cyclo(D-Cys-4-Pal-D-Trp-Lys-Cys)-Thr(Bzl)-Tyr-NH₂;
(T)aeg-cyclo(D-Cys-Tyr-D-Trp-Lys-Cys)-Thr(Bzl)-Tyr-NH₂;
(T)aeg-cyclo(D-Cys-Phe-D-Trp-Lys-Cys)-Thr(Bzl)-Tyr-NH₂;
15 (T)aeg-cyclo(D-Cys-(T)aeg-D-Trp-Lys-Cys)-Thr(Bzl)-Tyr-NH₂;
(T)aeg-cyclo(D-Cys-Pal-D-Trp-Lys-Cys)-Ser(Bzl)-Tyr-NH₂;
(T)aeg-cyclo(D-Cys-Pal-D-Trp-Lys-Cys)-Phe(4-O-Bzl)-Tyr-NH₂;
(T)aeg-cyclo(D-Cys-Pal-D-Trp-Lys-Cys)-A5c-Tyr-NH₂;
(T)aeg-cyclo(D-Cys-Pal-D-Trp-Lys-Cys)-Abu-Tyr-NH₂; or
20 D-Cpa-cyclo(D-Cys-(T)aeg-D-Trp-Lys-Cys)-Thr(Bzl)-Tyr-NH₂.

25. A pharmaceutical composition comprising an effective amount of a compound according to claim 1 or a pharmaceutically acceptable salt thereof and a pharmaceutically acceptable carrier.

25

26. A method of treating a disease in a subject, said method comprising administering to said subject a therapeutically effective amount of a compound of claim 1, wherein said disease is selected from the list consisting of lung cancer, glioma, anorexia, hypothyroidism,

- 80 -

hyperaldosteronism, H. pylori proliferation, acromegaly, restenosis, Crohn's disease, systemic sclerosis, external and internal pancreatic pseudocysts and ascites, VIPoma, nesidioblastosis, hyperinsulinism, gastrinoma, Zollinger-Ellison Syndrome, diarrhea, AIDS related diarrhea, chemotherapy related diarrhea, scleroderma, Irritable Bowel Syndrome, pancreatitis, small bowel obstruction, gastroesophageal reflux, duodenogastric reflux, Cushing's Syndrome, gonadotropinoma, hyperparathyroidism, Graves' Disease, diabetic neuropathy, Paget's disease, polycystic ovary disease, thyroid cancer, hepatome, leukemia, meningioma, cancer cachexia, orthostatic hypotension, postprandial hypotension, panic attacks, GH secreting adenomas, Acromegaly, TSH secreting adenomas, prolactin secreting adenomas, insulinoma, glucagonoma, diabetes mellitus, hyperlipidemia, insulin insensitivity, Syndrome X, angiopathy, proliferative retinopathy, dawn phenomenon, Nephropathy, gastric acid secretion, peptic ulcers, enterocutaneous fistula, pancreaticocutaneous fistula, Dumping syndrome, watery diarrhea syndrome, pancreatitis, gastrointestinal hormone secreting tumor, angiogenesis, arthritis, allograft rejection, graft vessel bleeding, portal hypertension, gastrointestinal bleeding, obesity, and opioid overdose.